



#14

SEQUENCE LISTING

<110> OXVIG, Claus
OVERGAARD, Michael T.

<120> PREGNANCY-ASSOCIATED PLASMA PROTEIN-A2 (PAPP-A2)

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<140> US 09/983,025
<141> 2001-10-22

<150> US 60/241,840
<151> 2000-10-20

<150> DK PA 2000 01571
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<170> PatentIn version 3.2

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Gly Trp Ala Leu Cys Ser Ala Asn Ser Glu Leu Gly Trp Thr Arg
      -215                -210                      -205

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Glu Gly Glu Arg Cys Trp Leu Gly Ala Lys Val Arg Arg Pro Arg
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Ala Ser Pro Gln His His Leu Phe Gly Val Tyr Pro Ser Arg Ala
 -170 -165 -160

Gly Asn Tyr Leu Arg Pro Tyr Pro Val Gly Glu Gln Glu Ile His
 -155 -150 -145

His Thr Gly Arg Ser Lys Pro Asp Thr Glu Gly Asn Ala Val Ser
 -140 -135 -130

Leu Val Pro Pro Asp Leu Thr Glu Asn Pro Ala Gly Leu Arg Gly
 -125 -120 -115

Ala Val Glu Glu Pro Ala Ala Pro Trp Val Gly Asp Ser Pro Ile
 -110 -105 -100

Gly Gln Ser Glu Leu Leu Gly Asp Asp Asp Ala Tyr Leu Gly Asn Gln
 -95 -90 -85

Arg Ser Lys Glu Ser Leu Gly Glu Ala Gly Ile Gln Lys Gly Ser Ala
 -80 -75 -70

Met Ala Ala Thr Thr Thr Thr Ala Ile Phe Thr Thr Leu Asn Glu Pro
 -65 -60 -55

Lys Pro Glu Thr Gln Arg Arg Gly Trp Ala Lys Ser Arg Gln Arg Arg
 -50 -45 -40 -35

Gln Val Trp Lys Arg Arg Ala Glu Asp Gly Gln Gly Asp Ser Gly Ile
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Tyr Arg Glu Ala Glu Thr Phe Asn Ser Gln Val Gly Leu Pro Ile Leu
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Cys	Ser	His	Thr	Val	Ser	Asp	Lys	Gly	Trp	Ala	Leu	Gly	Ile	Arg	Ser	80	85	90
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Asp	Glu	Lys	Tyr	Pro	Arg	Leu	Glu	Val	Leu	Gln	Gly	Phe	Glu	Pro	Glu	240	245	250

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Arg	Gly	Glu	Lys 290	Val	Ile	Arg	Tyr	Gln 295	Val	Val	Asn	Ile	Cys	Asp	Asp
Glu	Gly	Leu	Asn 305	Pro	Ile	Val	Ser 310	Glu	Glu	Gln	Ile	Arg 315	Leu	Gln	His
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Val	Asn	Cys	Glu	Pro 355	Ser	Lys	Ile	Gly	Asn 360	Asp	His	Cys	Asp	Pro	Glu 365
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Gly	Arg	Cys 385	Tyr	Ser	Trp	Asn	Arg 390	Arg	Asp	Gly	Leu	Cys 395	His	Val	Glu
Cys 400	Asn	Asn	Met	Leu	Asn	Asp 405	Phe	Asp	Asp	Gly	Asp 410	Cys	Cys	Asp	Pro
Gln 415	Val	Ala	Asp	Val	Arg 420	Lys	Thr	Cys	Phe	Asp 425	Pro	Asp	Ser	Pro	Lys 430
Arg	Ala	Tyr	Met	Ser 435	Val	Lys	Glu	Leu	Lys 440	Glu	Ala	Leu	Gln	Leu	Asn 445
Ser	Thr	His	Phe 450	Leu	Asn	Ile	Tyr	Phe 455	Ala	Ser	Ser	Val	Arg 460	Glu	Asp
Leu	Ala	Gly 465	Ala	Ala	Thr	Trp	Pro 470	Trp	Asp	Lys	Asp	Ala 475	Val	Thr	His
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Asp	Ser	Gln	Cys	Val	Leu	Asn	Cys	Asn	Gln	Glu	Arg	Glu	Lys	Leu
			1385					1390					1395	

Pro	Ile	Leu	Cys	Thr	Lys	Glu	Gly	Leu	Trp	Thr	Gln	Glu	Phe	Lys
			1400					1405					1410	
Leu	Cys	Glu	Asn	Leu	Gln	Gly	Glu	Cys	Pro	Pro	Pro	Pro	Ser	Glu
			1415					1420					1425	
Leu	Asn	Ser	Val	Glu	Tyr	Lys	Cys	Glu	Gln	Gly	Tyr	Gly	Ile	Gly
			1430					1435					1440	
Ala	Val	Cys	Ser	Pro	Leu	Cys	Val	Ile	Pro	Pro	Ser	Asp	Pro	Val
			1445					1450					1455	
Met	Leu	Pro	Glu	Asn	Ile	Thr	Ala	Asp	Thr	Leu	Glu	His	Trp	Met
			1460					1465					1470	
Glu	Pro	Val	Lys	Val	Gln	Ser	Ile	Val	Cys	Thr	Gly	Arg	Arg	Gln
			1475					1480					1485	
Trp	His	Pro	Asp	Pro	Val	Leu	Val	His	Cys	Ile	Gln	Ser	Cys	Glu
			1490					1495					1500	
Pro	Phe	Gln	Ala	Asp	Gly	Trp	Cys	Asp	Thr	Ile	Asn	Asn	Arg	Ala
			1505					1510					1515	
Tyr	Cys	His	Tyr	Asp	Gly	Gly	Asp	Cys	Cys	Ser	Ser	Thr	Leu	Ser
			1520					1525					1530	
Ser	Lys	Lys	Val	Ile	Pro	Phe	Ala	Ala	Asp	Cys	Asp	Leu	Asp	Glu
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Cys	Thr	Cys	Arg	Asp	Pro	Lys	Ala	Glu	Glu	Asn	Gln			
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22

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<223> primer PR-N5

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23

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21

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25

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22

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33

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26

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Lys Leu Gly Pro
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Glu Gln Lys Leu Ile Ser Glu Glu Asp Leu
1 5 10

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Asn Ser Ala Val Asp

1 5

<210> 21

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<213> Artificial Sequence

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30

<210> 22

<211> 29

<212> DNA

<213> Artificial Sequence

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<223> primer containing HindIII site, for amplifying IGFBP-5 cDNA

<400> 22

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29

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<212> PRT

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<210> 24

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digested with PAPP-A2

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 20 25 30

Arg Ala Gly Arg Pro Pro Arg Pro Ala Ala Gly Pro Ala Thr Cys Ala
 35 40 45

Thr Arg Gly Pro Arg Pro Pro Arg Leu Ala Ala Ala Ala Ala Ala
 50 55 60

Gly Arg Ala Trp Glu Ala Val Arg Val Pro Arg Arg Arg Gln Gln Arg
 65 70 75 80

Glu Ala Arg Gly Ala Thr Glu Glu Pro Ser Pro Pro Ser Arg Ala Leu
 85 90 95

Tyr Phe Ser Gly Arg Gly Glu Gln Leu Arg Val Leu Arg Ala Asp Leu
 100 105 110

Glu Leu Pro Arg Asp Ala Phe Thr Leu Gln Val Trp Leu Arg Ala Glu
 115 120 125

Gly Gly Gln Arg Ser Pro Ala Val Ile Thr Gly Leu Tyr Asp Lys Cys
 130 135 140

Ser Tyr Ile Ser Arg Asp Arg Gly Trp Val Val Gly Ile His Thr Ile
 145 150 155 160

Ser	Asp	Gln	Asp	Asn	Lys	Asp	Pro	Arg	Tyr	Phe	Phe	Ser	Leu	Lys	Thr			
				165					170					175				
Asp	Arg	Ala	Arg	Gln	Val	Thr	Thr	Ile	Asn	Ala	His	Arg	Ser	Tyr	Leu			
				180				185					190					
Pro	Gly	Gln	Trp	Val	Tyr	Leu	Ala	Ala	Thr	Tyr	Asp	Gly	Gln	Phe	Met			
		195					200					205						
Lys	Leu	Tyr	Val	Asn	Gly	Ala	Gln	Val	Ala	Thr	Ser	Gly	Glu	Gln	Val			
	210					215					220							
Gly	Gly	Ile	Phe	Ser	Pro	Leu	Thr	Gln	Lys	Cys	Lys	Val	Leu	Met	Leu			
225					230					235					240			
Gly	Gly	Ser	Ala	Leu	Asn	His	Asn	Tyr	Arg	Gly	Tyr	Ile	Glu	His	Phe			
				245					250					255				
Ser	Leu	Trp	Lys	Val	Ala	Arg	Thr	Gln	Arg	Glu	Ile	Leu	Ser	Asp	Met			
			260					265					270					
Glu	Thr	His	Gly	Ala	His	Thr	Ala	Leu	Pro	Gln	Leu	Leu	Leu	Gln	Glu			
		275					280					285						
Asn	Trp	Asp	Asn	Val	Lys	His	Ala	Trp	Ser	Pro	Met	Lys	Asp	Gly	Ser			
	290					295					300							
Ser	Pro	Lys	Val	Glu	Phe	Ser	Asn	Ala	His	Gly	Phe	Leu	Leu	Asp	Thr			
305					310					315					320			
Ser	Leu	Glu	Pro	Pro	Leu	Cys	Gly	Gln	Thr	Leu	Cys	Asp	Asn	Thr	Glu			
				325					330					335				
Val	Ile	Ala	Ser	Tyr	Asn	Gln	Leu	Ser	Ser	Phe	Arg	Gln	Pro	Lys	Val			
			340					345					350					
Val	Arg	Tyr	Arg	Val	Val	Asn	Leu	Tyr	Glu	Asp	Asp	His	Lys	Asn	Pro			
		355					360					365						
Thr	Val	Thr	Arg	Glu	Gln	Val	Asp	Phe	Gln	His	His	Gln	Leu	Ala	Glu			
	370					375					380							

Ala Phe Lys Gln Tyr Asn Ile Ser Trp Glu Leu Asp Val Leu Glu Val
385 390 395 400

Ser Asn Ser Ser Leu Arg Arg Arg Leu Ile Leu Ala Asn Cys Asp Ile
405 410 415

Ser Lys Ile Gly Asp Glu Asn Cys Asp Pro Glu Cys Asn His Thr Leu
420 425 430

Thr Gly His Asp Gly Gly Asp Cys Arg His Leu Arg His Pro Ala Phe
435 440 445

Val Lys Lys Gln His Asn Gly Val Cys Asp Met Asp Cys Asn Tyr Glu
450 455 460

Arg Phe Asn Phe Asp Gly Gly Glu Cys Cys Asp Pro Glu Ile Thr Asn
465 470 475 480

Val Thr Gln Thr Cys Phe Asp Pro Asp Ser Pro His Arg Ala Tyr Leu
485 490 495

Asp Val Asn Glu Leu Lys Asn Ile Leu Lys Leu Asp Gly Ser Thr His
500 505 510

Leu Asn Ile Phe Phe Ala Lys Ser Ser Glu Glu Glu Leu Ala Gly Val
515 520 525

Ala Thr Trp Pro Trp Asp Lys Glu Ala Leu Met His Leu Gly Gly Ile
530 535 540

Val Leu Asn Pro Ser Phe Tyr Gly Met Pro Gly His Thr His Thr Met
545 550 555 560

Ile His Glu Ile Gly His Ser Leu Gly Leu Tyr His Val Phe Arg Gly
565 570 575

Ile Ser Glu Ile Gln Ser Cys Ser Asp Pro Cys Met Glu Thr Glu Pro
580 585 590

Ser Phe Glu Thr Gly Asp Leu Cys Asn Asp Thr Asn Pro Ala Pro Lys
595 600 605

His Lys Ser Cys Gly Asp Pro Gly Pro Gly Asn Asp Thr Cys Gly Phe
610 615 620

His 625	Ser	Phe	Phe	Asn	Thr 630	Pro	Tyr	Asn	Asn	Phe 635	Met	Ser	Tyr	Ala	Asp 640
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Cys	Tyr	Leu	Asp 660	Leu	Val	Tyr	Gln	Gly 665	Trp	Gln	Pro	Ser	Arg	Lys	Pro 670
Ala	Pro	Val	Ala	Leu	Ala	Pro	Gln 680	Val	Leu	Gly	His	Thr 685	Thr	Asp	Ser
Val 690	Thr	Leu	Glu	Trp	Phe	Pro 695	Pro	Ile	Asp	Gly	His	Phe	Phe	Glu	Arg
Glu 705	Leu	Gly	Ser	Ala	Cys 710	His	Leu	Cys	Leu	Glu 715	Gly	Arg	Ile	Leu	Val 720
Gln	Tyr	Ala	Ser	Asn 725	Ala	Ser	Ser	Pro	Met 730	Pro	Cys	Ser	Pro	Ser	Gly 735
His	Trp	Ser 740	Pro	Arg	Glu	Ala	Glu	Gly 745	His	Pro	Asp	Val	Glu	Gln	Pro 750
Cys	Lys	Ser 755	Ser	Val	Arg	Thr	Trp 760	Ser	Pro	Asn	Ser	Ala	Val	Asn	Pro 765
His 770	Thr	Val	Pro	Pro	Ala	Cys 775	Pro	Glu	Pro	Gln	Gly 780	Cys	Tyr	Leu	Glu
Leu 785	Glu	Phe	Leu	Tyr	Pro 790	Leu	Val	Pro	Glu	Ser 795	Leu	Thr	Ile	Trp	Val 800
Thr	Phe	Val	Ser	Thr 805	Asp	Trp	Asp	Ser	Ser	Gly	Ala	Val	Asn	Asp	Ile 815
Lys	Leu	Leu	Ala	Val	Ser	Gly	Lys	Asn 825	Ile	Ser	Leu	Gly	Pro	Gln	Asn 830
Val 835	Phe	Cys	Asp	Val	Pro	Leu	Thr 840	Ile	Arg	Leu	Trp	Asp 845	Val	Gly	Glu

Glu Val Tyr Gly Ile Gln Ile Tyr Thr Leu Asp Glu His Leu Glu Ile
850 855 860

Asp Ala Ala Met Leu Thr Ser Thr Ala Asp Thr Pro Leu Cys Leu Gln
865 870 875 880

Cys Lys Pro Leu Lys Tyr Lys Val Val Arg Asp Pro Pro Leu Gln Met
885 890 895

Asp Val Ala Ser Ile Leu His Leu Asn Arg Lys Phe Val Asp Met Asp
900 905 910

Leu Asn Leu Gly Ser Val Tyr Gln Tyr Trp Val Ile Thr Ile Ser Gly
915 920 925

Thr Glu Glu Ser Glu Pro Ser Pro Ala Val Thr Tyr Ile His Gly Arg
930 935 940

Gly Tyr Cys Gly Asp Gly Ile Ile Gln Lys Asp Gln Gly Glu Gln Cys
945 950 955 960

Asp Asp Met Asn Lys Ile Asn Gly Asp Gly Cys Ser Leu Phe Cys Arg
965 970 975

Gln Glu Val Ser Phe Asn Cys Ile Asp Glu Pro Ser Arg Cys Tyr Phe
980 985 990

His Asp Gly Asp Gly Val Cys Glu Glu Phe Glu Gln Lys Thr Ser Ile
995 1000 1005

Lys Asp Cys Gly Val Tyr Thr Pro Gln Gly Phe Leu Asp Gln Trp
1010 1015 1020

Ala Ser Asn Ala Ser Val Ser His Gln Asp Gln Gln Cys Pro Gly
1025 1030 1035

Trp Val Ile Ile Gly Gln Pro Ala Ala Ser Gln Val Cys Arg Thr
1040 1045 1050

Lys Val Ile Asp Leu Ser Glu Gly Ile Ser Gln His Ala Trp Tyr
1055 1060 1065

Pro Cys Thr Ile Ser Tyr Pro Tyr Ser Gln Leu Ala Gln Thr Thr
1070 1075 1080

Phe	Trp	Leu	Arg	Ala	Tyr	Phe	Ser	Gln	Pro	Met	Val	Ala	Ala	Ala
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Val	Ile	Val	His	Leu	Val	Thr	Asp	Gly	Thr	Tyr	Tyr	Gly	Asp	Gln
1100						1105					1110			
Lys	Gln	Glu	Thr	Ile	Ser	Val	Gln	Leu	Leu	Asp	Thr	Lys	Asp	Gln
1115						1120					1125			
Ser	His	Asp	Leu	Gly	Leu	His	Val	Leu	Ser	Cys	Arg	Asn	Asn	Pro
1130						1135					1140			
Leu	Ile	Ile	Pro	Val	Val	His	Asp	Leu	Ser	Gln	Pro	Phe	Tyr	His
1145						1150					1155			
Ser	Gln	Ala	Val	Arg	Val	Ser	Phe	Ser	Ser	Pro	Leu	Val	Ala	Ile
1160						1165					1170			
Ser	Gly	Val	Ala	Leu	Arg	Ser	Phe	Asp	Asn	Phe	Asp	Pro	Val	Thr
1175						1180					1185			
Leu	Ser	Ser	Cys	Gln	Arg	Gly	Glu	Thr	Tyr	Ser	Pro	Ala	Glu	Gln
1190						1195					1200			
Ser	Cys	Val	His	Phe	Ala	Cys	Glu	Lys	Thr	Asp	Cys	Pro	Glu	Leu
1205						1210					1215			
Ala	Val	Glu	Asn	Ala	Ser	Leu	Asn	Cys	Ser	Ser	Ser	Asp	Arg	Tyr
1220						1225					1230			
His	Gly	Ala	Gln	Cys	Thr	Val	Ser	Cys	Arg	Thr	Gly	Tyr	Val	Leu
1235						1240					1245			
Gln	Ile	Arg	Arg	Asp	Asp	Glu	Leu	Ile	Lys	Ser	Gln	Thr	Gly	Pro
1250						1255					1260			
Ser	Val	Thr	Val	Thr	Cys	Thr	Glu	Gly	Lys	Trp	Asn	Lys	Gln	Val
1265						1270					1275			
Ala	Cys	Glu	Pro	Val	Asp	Cys	Ser	Ile	Pro	Asp	His	His	Gln	Val
1280						1285					1290			

Tyr Ala Ala Ser Phe Ser Cys Pro Glu Gly Thr Thr Phe Gly Ser
1295 1300 1305

Gln Cys Ser Phe Gln Cys Arg His Pro Ala Gln Leu Lys Gly Asn
1310 1315 1320

Asn Ser Leu Leu Thr Cys Met Glu Asp Gly Leu Trp Ser Phe Pro
1325 1330 1335

Glu Ala Leu Cys Glu Leu Met Cys Leu Ala Pro Pro Pro Val Pro
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Asn Ala Asp Leu Gln Thr Ala Arg Cys Arg Glu Asn Lys His Lys
1355 1360 1365

Val Gly Ser Phe Cys Lys Tyr Lys Cys Lys Pro Gly Tyr His Val
1370 1375 1380

Pro Gly Ser Ser Arg Lys Ser Lys Lys Arg Ala Phe Lys Thr Gln
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Cys Thr Gln Asp Gly Ser Trp Gln Glu Gly Ala Cys Val Pro Val
1400 1405 1410

Thr Cys Asp Pro Pro Pro Pro Lys Phe His Gly Leu Tyr Gln Cys
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Thr Asn Gly Phe Gln Phe Asn Ser Glu Cys Arg Ile Lys Cys Glu
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Asp Ser Asp Ala Ser Gln Gly Leu Gly Ser Asn Val Ile His Cys
1445 1450 1455

Arg Lys Asp Gly Thr Trp Asn Gly Ser Phe His Val Cys Gln Glu
1460 1465 1470

Met Gln Gly Gln Cys Ser Val Pro Asn Glu Leu Asn Ser Asn Leu
1475 1480 1485

Lys Leu Gln Cys Pro Asp Gly Tyr Ala Ile Gly Ser Glu Cys Ala
1490 1495 1500

Thr Ser Cys Leu Asp His Asn Ser Glu Ser Ile Ile Leu Pro Met
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Asn Val Thr Val Arg Asp Ile Pro His Trp Leu Asn Pro Thr Arg
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 Val Glu Arg Val Val Cys Thr Ala Gly Leu Lys Trp Tyr Pro His
 1535 1540 1545
 Pro Ala Leu Ile His Cys Val Lys Gly Cys Glu Pro Phe Met Gly
 1550 1555 1560
 Asp Asn Tyr Cys Asp Ala Ile Asn Asn Arg Ala Phe Cys Asn Tyr
 1565 1570 1575
 Asp Gly Gly Asp Cys Cys Thr Ser Thr Val Lys Thr Lys Lys Val
 1580 1585 1590
 Thr Pro Phe Pro Met Ser Cys Asp Leu Gln Gly Asp Cys Ala Cys
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